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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/787,612	03/20/2001	Kanji Takada	AKA-269	4679

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 09/22/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/787,612	TAKADA, KANJI	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-19 and 27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-19 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION.

Claims 10-19 and 27 are pending in this application. Claims 1-9 stand cancelled and claims 20-26 are withdrawn as being directed to a non-elected invention.

In view of the Appeal Brief filed on 6/24/05, PROSECUTION IS HEREBY REOPENED. A New Ground of Rejections is set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

(1) file a reply under 37 CFR 1.111 (if this Office action is non-final) or a reply under 37 CFR 1.113 (if this Office action is final); or,

(2) initiate a new appeal by filing a notice of appeal under 37 CFR 41.31 followed by an appeal brief under 37 CFR 41.37. The previously paid notice of appeal fee and appeal brief fee can be applied to the new appeal. If, however, the appeal fees set forth in 37 CFR 41.20 have been increased since they were previously paid, then appellant must pay the difference between the increased fees and the amount previously paid.

A Supervisory Patent Examiner (SPE) has approved of reopening prosecution by signing below.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 10-19 and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "sufficient" in independent claims 10, 19, and 27 is a relative term which renders the claim indefinite. The term sufficient is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 10-12, 14, 16-19, and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 03-255037 (entire document) to Morita et al in view of Okada et al (6,113,943) in further view of Watts (6,228,396).

Morita et al teach a glycyrrhizin preparation blended with fatty acid glycerides and coated with an enteric (releases in the intestines) film to form capsules. See abstract. The fatty acid glycerides taught are monoglycerides, diglycerides, and triglycerides of fatty acids such as stearic acid, caprylic acid, and capric acid. See page 3, third paragraph of translation. The enteric

film polymers that are taught are hydroxypropylmethylcellulose phthalate, cellulose acetates, and hydroxypropylmethylcellulose acetate succinate. See page 3 of translation. The ratio of glycyrrhizin to fatty acid glycerides if 10:1 to 1:100. See page 3, last paragraph of translation. The preparation may further contains a lubricant, stabilizer, **surfactant**, a solubilizing aid, and melting point adjusting agent. See page 3, sixth paragraph. Lastly, Morita teaches a dose of 10-500mg of glycyrrhizin. See examples and page 4, second paragraph.

Morita does not teach the instant ethylcellulose coating.

Okada et al teach a sustained release preparation capable of releasing an active agent. See abstract. Okada teaches the sustained release preparations may be in various forms such as capsules, tablets, and suppositories (made of a fatty acid glycerides). See column 18, lines 45-50 and column 19, lines 40-20. Further, Okada teaches that an oral preparation may be produced by adding an excipients such as binders, a lubricant, etc, followed by coating to confer an enteric or sustained-release property by a per se known method when necessary. Okada teaches examples of coating agents include hydroxypropylmethylcellulose, **ethylcellulose**, cellulose acetate phthalate, **hydroxypropylmethylcellulose phthalate**, and hydroxymethylcellulose acetate succinate, among others. See column 19, lines 9-25.

Watts teaches a colonic delivery device wherein the composition is delivered to the colon. See abstract. *Any* coating can be used which ensures that the capsule does not break-up and release the drug until it is in the colon. The thickness of the coating will typically be in the range of 80 microns 300 microns. The thickness of the particular coating used will be chosen according to the mechanism by which the coating is dissolved. Preferred coating materials are those which dissolve at a pH of 5 or above. The coatings therefore only begin to dissolve when

they have left the stomach and entered the small intestine. A thick layer of coating is provided which will dissolve in about 3-4 hours thereby allowing **the capsule underneath to breakup only when it has reached the terminal ileum or the colon.** Such a coating can be made from a variety of polymers such as cellulose acetate trimellitate (CAT), **hydroxypropylmethyl cellulose phthalate** (HPMCP), polyvinyl acetate phthalate (PVAP), **cellulose acetate phthalate** (CAP) and shellac as described by Healy in his article "Enteric Coatings and Delayed Release" Chapter 7 in Drug Delivery to the Gastrointestinal Tract, editors Hardy et al., Ellis Horwood, Chichester, 1989.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Morita et al and Okada et al and substitute Morita's hydroxypropylmethylcellulose phthalate coating with the instant ethylcellulose coating. One would have been motivated to do so since Okada teaches both Morita's hydroxypropylmethylcellulose phthalate and instantly claimed ethylcellulose are polymers used for forming enteric coatings. Thus, a skilled artisan would have expected similar results by utilizing instant ethycellulose as the polymer of choice since the prior art clearly establishes the functional equivalency of ethylcellulose and hydroxypropylmethylcellulose phthalate. It is considered prima facie obvious to substitute equivalents known for the same purpose absent evidence indicating the criticality of the instant polymer.

The examiner relies on Watts to further show that all enteric coating polymers including Morita's hydroxypropylmethylcellulose phthalate have the implicit ability to cause the core to "rupture"; in other words, Watt's shows that Morita's polymer functions in the same manner as the instantly claimed ethylcellulose. Therefore, a skilled artisan would have expected similar

results utilizing *either* enteric polymer with the expectation of ruptured release in the intestine. It should also be noted "where the claimed and prior art products are identical or *substantially identical* in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established." See In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, **the applicant has the burden of showing that they are not**." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Lastly, Watts demonstrates that determining thickness is a routine skill in the art wherein a skilled artisan would utilize a particular thickness depending on the desired area of release in the intestine. It should be further noted that the recitation of "sufficient thickness" is rejected under indefiniteness since the specification does not provide a definition of "sufficient thickness".

With regard to the recitation "glyceride that melts or liquefies at body temperature", the examiner points out that this is an inherent feature of the fatty acid glycerides taught in Morita. The examiner cites US 4,717,566 as art of interest. Eckenhoff teaches thermo-responsive compositions that are capable of softening, or becoming dispensable in response to heat and hardening again when cooled. Eckenhoff teaches that carrier must exhibit solid, or solid-like properties at temperatures up to 31.degree. C., and become fluid, semisolid, or viscous when disturbed by heat at temperatures from 31.degree. C., and usually in the range of 31.degree. C. to 45.degree. C. The thermo-responsive carriers taught include mono, di, triglycerides of acid having from 8-22 carbons...including stearic [acid]." See column 11, lines 25-65.

With regard to the process-by-product limitations of claims 12, "even though product by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production, [i]f the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior art was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed.Cir. 1985). See MPEP section 2113.

Claims 13 and 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over JP 03-255037 to Morita et al in view of Okada et al (6,113,943) in further view of in view of Sipos (4079125).

The teachings of Morita et al and Okada et al have been set forth above in detail. Morita et al teach a glycyrrhizin preparation blended with fatty acid glycerides and coated with an enteric film to form capsules. Okada teaches the functional equivalency of the instantly claimed enteric polymer and that of Morita.

The references do not teach the limitation of claim 13 and 15.

Sipos teaches an enteric coating for the delivery of drugs to the intestinal region. In the enteric coat method, Sipos teaches dusting talc on the tablet to prevent aggregation of the tablet (col. 8, line 65 to col. 9, line 4). Further, Sipos teaches enteric coating methods are well known in the art (col. 9, lines 1-4).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings the above references and dust the device with talc before

coating it. One would have bee motivated to do so since dusting the oral preparation with talc prevents aggregation of the tablet during the coating method ,as taught by Sipos.

Claims 1-19 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Takada (5637319) in view of JP 03-255037 (entire document) in view of Tolstikov et al (Bioorg Khim. 1989 March; 15(3):392-8) in further view of Morita et al .

Takada teaches an oral controlled release preparation (capsule) to deliver drugs to the lower gastrointestinal tract. The reference teaches the suitability of the dosage form for drugs that need to be delivered to the lower part of the small intestine and/or colon and is especially suitable for drugs that are not to be released in the upper part of the GI tract. See column 3, lines 58-63 and column 5, lines 40-43. The dosage form allows for a sustained release and the gastrointestinal cells are exposed to high concentration of the drug (col. 3, lines 35-50). Takada teaches an ethyl cellulose covered capsule containing a drug composition (Fig. 9). The reference teaches that the thickness of the water soluble membrane and the intestinal pressure control the release of the material so that the delivery system is site specific and delivers the drug to the large intestine (Note abstract). The preparation allows (1) the delivery of protein/peptide drugs and drugs for the treatment of IBD to the lower GI tract by releasing them to lower part of the intestine like lower parts of small intestine, colon and so forth, (2) the release of drugs such as anti-cancer drug, **anti-inflammatory drug** and anti-asthmatic drugs etc. at a constant rate during its passage through the GI tract, and (3) sustained-release profiles by combining a fast-release tablet or capsule and a delayed-release tablet or capsule. See column 4, lines 1-10. Takada teaches the use of **anti-inflammatory** like methylprednisolone for inflammatory bowel disease (IBD). See column 5, lines 40-45.

Takada does not teach the instant drug or fatty acid glycerides.

Tolstikov et al teach glycyrrhizin acid derivatives possess high predinsolone like anti-inflammatory active and display pronounced stimulative effect on humoral factors of immunity. See abstract.

Morita et al teach a glycyrrhizin preparation blended with fatty acid glycerides and coated with an enteric (releases in the intestines) film to form capsules. See abstract. Morita teaches the use of glycyrrhizin to treat liver disease and inflammatory disorders. See page 2. The fatty acid glycerides taught are monoglycerides, diglycerides, and triglycerides of fatty acids such as stearic acid, caprylic acid, and capric acid. The fatty acid glycerides are taught increase absorption of glycyrrhizin. See page 3, third paragraph of translation. The enteric film polymers that are taught are hydroxypropylmethylcellulose phthalate, cellulose acetates, and hydroxypropylmethylcellulose acetate succinate. See page 3 of translation. The enteric film is taught for the release of glycyrrhizin in the intestines since the absorption is the greatest in this region. The ratio of glycyrrhizin to fatty acid glycerides if 10:1 to 1:100. See page 3, last paragraph of translation. The preparation may further contains a lubricant, stabilizer, **surfactant**, a solubilizing aid, and melting point adjusting agent. See page 3, sixth paragraph. Lastly, Morita teaches a dose of 10-500mg of glycyrrhizin. See examples and page 4, second paragraph.

Firstly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Takada et al and Tolstikov and use the instantly claimed glycyrrhizin as the active agent of choice in Takada's invention. One would have been motivated to do so since Tolstikov teaches instant glycyrrhizin is an effective anti-inflammatory agent with an anti-inflammatory action akin to predinsolone and Takada teaches the

ethylcellulose coated device is useful for drugs such as anti-inflammatory agents. Furthermore, Takada teaches the use of methylpredinsolone as a possible agent to treat IBD. Therefore, one would have reasonably expected success since the prior art teaches that glycyrrhizin is an anti-inflammatory agent and has effects similar to the Takada's specified drug predinosolone.

Secondly, one would have been motivated to look to Morita who also teaches the glycyrrhizin for inflammatory disorders, and utilize fatty acid glycerides since Morita teaches the use of fatty acid glycerides allow glycyrrhizin to be absorbed rapidly in the intestine because the glycerides provide surface activity. Thus, one would have been motivated to use a glyceride base to increase the absorption of glycyrrhizin. Lastly, one would have reasonably expected similar results by using glycyrrhizin in Takada's device since Morita teaches glycyrrhizin is effectively absorbed in intestine and Takada's device is targeted for release in the lower intestine.

With regard to the recitation of "sufficient thickness", this term is rejected under indefiniteness since the specification does not provide a definition of "sufficient thickness".

With regard to the recitation "glyceride that melts or liquefies at body temperature", the examiner points out that this is an inherent feature of the fatty acid glycerides taught in Morita. The examiner cites US 4,717,566 as art of interest. Eckenhoff teaches thermo-responsive compositions that are capable of softening, or becoming dispensable in response to heat and hardening again when cooled. Eckenhoff teaches that carrier must exhibit solid, or solid-like properties at temperatures up to 31.degree. C., and become fluid, semisolid, or viscous when disturbed by heat at temperatures from 31.degree. C., and usually in the range of 31.degree. C. to 45.degree. C. The thermo-responsive carriers taught include mono, di, triglycerides of acid having from 8-22 carbons...including stearic [acid]." See column 11, lines 25-65.

With regard to the process-by-product limitations of claims 12, "even though product by process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production, [i]f the product in the product-by-process claim is the same or obvious from a product of the prior art, the claim is unpatentable even though the prior art was made by a different process." *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed.Cir. 1985). See MPEP section 2113.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 10-19 and 27 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims of U.S. Patent No. 6,890,547. Although the conflicting claims are not identical, they are not patentably distinct from each other because both are directed to similar subject matter.

Instant application is directed to a device for colon-targeted oral delivery of glycyrrhizin comprising a shaped core containing an amount of glycyrrhizin, said shaped core being made of a suppository base comprising glyceride that melts or liquefies at the body temperature, and a

coating film of ethylcellulose enclosing said shaped core and having a film thickness whereby when the device is transported through the digestive tract to the colon, the film enclosing the liquefied core ruptures selectively in the colon by the internal pressure generated by the peristalsis of the intestine.

US '547 is directed to a glycyrrhizin oral preparation in a form of a capsule for transmucosal absorption which comprises glycyrrhizin and an ester mixture of a C.sub.6-18 fatty acid glycerol ester with a C.sub.1-18 fatty acid macrogol ester in a weight ratio of the glycyrrhizin to the ester mixture being 1:0.05 to 1:10, wherein the capsule is made of a high-molecular polymer which is not degraded or dissolved in a digestive tract, or which is made of gelatin lined with said polymer, and wherein the capsule is collapsed by internal pressure in a large intestine to release the glycyrrhizin. Dependent claim 2 is directed to the glycyrrhizin preparation for transmucosal absorption according to claim 1, wherein the C.sub.6-18 fatty acid is a saturated fatty acid. Dependent claim 5 is directed to the glycyrrhizin preparation for transmucosal absorption according to claim 1, which further comprises an organic acid, a chelating agent or a surfactant. Note that the specification defines the "high molecular polymer" as ethylcellulose. Se column 5, lines 39-40.

The instant claims anticipate the subject matter of US '547 since the instant claims are directed to the broad scope and US '547 is directed to the narrow scope wherein the composition has fatty acids glycerides (fatty acid glycerol ester) and macrogel esters. The instant claim language is open-ended claim language and thus can comprise the "macrogel esters" in US '547.

Conclusion

All the claims are rejected.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US 6,326,360 to Kanazawa et al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616

SSG

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER